REMARKS

Applicants respectfully request reconsideration. Claims 1-36 were previously pending in this application. Claims 15-36 are withdrawn from consideration. By this amendment, Applicants are cancelling claim 8 without prejudice or disclaimer. Claim 1 has been amended. As a result, claims 1-7 and 9-14 are pending for examination with claim 1 being an independent claim. No new matter has been added.

Support for the subject matter added to amended claim 1 is found, e.g., in original claim 8 of the specification.

Applicants therefore respectfully request reconsideration of the claims, all of which are in condition for allowance as noted below.

As a preliminary matter, Applicants also request that paragraph [0081] of U.S. patent application Publication No. 2006/0188563 (also page 26, first full paragraph of the specification as filed) be replaced as indicated above. Applicants kindly note that no new matter has been added and that this amendment is made only to correct an obvious error, which is easily recognized by one skilled in the art. See, M.P.E.P. § 2163.07 (*In re Odd*, 443 F.2d 1200, 170 USPQ 268 (CCPA 1971)). One having skill in the art would certainly recognize that a "formulation of the core when budesonide is used," see paragraph [0081], would contain budesonide, and not fluoroucil.

This is especially true in view of the rest of the specification, which recites in part a paragraph that lists fluorouracil and budesonide as among several not limiting but exemplary pharmacologically active ingredients that may be used in the core. See paragraph [0077] of the published application. Immediately thereafter, two paragraphs more particularly recite exemplary amounts of only fluorouracil. See paragraphs [0078] and [0079]. Then, in the same paragraph format as paragraphs [0078] and [0079], two paragraphs particularly recite exemplary amounts of

budesonide. See paragraphs [0080] and [0081]. As seen by the logical flow of paragraphs [0077]-[0081], and the pattern established by paragraphs [0078] and [0079], the last two paragraphs [0080] and [0081] should recite only budesonide, not fluorouracil.

Rejections Under 35 U.S.C. § 102

The Examiner rejected claims 1-4, 7, 12 and 13 under 35 U.S.C. § 102(b) as being anticipated by Tanida et al. (U.S. Patent No. 6,214,378) ("Tanida").

The Examiner also rejected claims 1-4, 7 and 13 under 35 U.S.C. § 102(b) as being anticipated by Okayama et al. (U.S. Patent No. 5,654,004) ("Okayama").

Applicants respectfully traverse these rejections in view of the amendment of claim 1. Applicants respectfully submit that neither of the references disclose, suggest, or predict the preparation recited in amended claim 1 or the dependent claims. The prior art references must teach or suggest all of the particular limitations of the claims. *In re Wilson*, 424 F.2d 1382, 1385 (CCPA 1970); *In re Royka*, 490 F.2d 981 (CCPA 1974); *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236 (Fed. Cir. 1989) ("The identical invention must be shown in as complete detail as is contained in the...claim.").

With regard to a medicinal oral preparation designed so that "in a disintegration test comprising vertical movement for 2 hours in a first solution of pH 1.2, subsequent vertical movement for 2 hours in a second solution of pH 7.4, and final vertical movement in a third solution of pH 6.4, the average disintegration initiation time and the average disintegration completion time each fall within a period from 35 min to 130 min after starting the vertical movement in the third solution", Applicants respectfully submit that various embodiments of the claimed invention, which exhibit these properties, are compositionally different from the preparations taught by Tanida and Okayama.

Applicants appreciate the USPTO's inability to test properties, and as evidence for this submission first note that the claimed properties are indicative of, for example, core and core-to-outside layer feature(s), not taught by the prior art. The specification generally points to "properties of the formulated core," first line of paragraph [0006] of the published application, as expressed in part by the disintegration properties of the preparation, *see* paragraph [0009]. As a result, the claimed properties indicate novel and non-obvious structural feature(s) of the preparation in claim 1, not previously known in regard to "conventional medicinal oral preparation for colon delivery comprising two polymer coating layers covering a core[.]" *See* paragraph [0011].

The problem recognized and solved in the claimed invention therefore illustrates the complexity of making a suitable preparation for appropriate disintegration at, and thus delivery of a substance to, a colon. In addition to numerous external variations in pH and time traveled due to person-to-person physiological and dietary variances (which change even from moment to moment), the multiple-layered components in such preparations present a quite complex and extremely unpredictable variable matrix, for which workable results are not obtained by simple optimization.

Several embodiments of such preparations are more particularly claimed in terms of the weight ratios of the inner and outer layers with respect to the core (claims 5 and 6), core weight percentage of a disintegrating agent (previous claim 8), core weight percentage of the amino and organic acids (claims 9-11), and the core diameter and thickness (claim 14).

Specifically regarding previous claim 8, none of the references teach 3-15 weight % of any of the disintegrating agents now added to claim 1. *See* previous claim 8 ("crospovidone, pregelatinized starch, sodium carboxymethyl starch, carmellose, calcium carmellose, sodium carmellose, powdered agar, sodium croscarmellose, low-substituted hydroxypropyl cellulose, starch, dextrin, hydroxyethylmethyl cellulose, carboxymethyl cellulose, hydroxypropyl starch, Macrogol,

and mannitol."); *compare* with Tanida's Eudragit E and Eudragit S, which are not in previous claim 8, at 7%; and crospovidone at 50% by weight.

Thus, neither Tanida nor Okayama disclose a preparation characterized by the features as claimed. Accordingly, withdrawal of this rejection is respectfully requested.

Rejections Under 35 U.S.C. § 103

The Examiner rejected claims 1-14 under 35 U.S.C. § 103(a) as being unpatentable over Tanida et al. (U.S. Patent No. 6,214,378) ("Tanida") in view of Adesunloye et al. (U.S. Patent No. 5,874,106) ("Adesunloye") with respect to claims 9-11. Applicants respectfully traverse the rejection in view of the amendment made to claim 1.

Applicants respectfully submit that the combination of the cited references does not disclose, suggest, or predict the preparation recited in amended claim 1 or claims dependent therefrom because the references all fail to disclose the limitations noted above from claim 1.

Tanida and Adesunloye also fail to recognize that the above-mentioned claim limitations or particular compositional properties are result-effective variables, which in particular affect average disintegration initiation and completion times. MPEP § 2144.05(II) states:

> A particular parameter must first be recognized as a result-effective variable, i.e., a variable which achieves a recognized result, before the determination of the optimum or workable ranges of said variable might be characterized as routine experimentation. *In re Antonie*, 559 F.2d 618, 195 USPQ 6 (CCPA 1977) (The claimed wastewater treatment device had a tank volume to contractor area of 0.12 gal./sq. ft. The prior art did not recognize that treatment capacity is a function of the tank volume to contractor ratio, and therefore the parameter optimized was not recognized in the art to be a result-effective variable). See also *In re Boesch*, 617 F.2d 272, 205 USPQ 215 (CCPA 1980) (prior art suggested proportional balancing to achieve desired results in the formation of an alloy).

The combination of Tanida and Adesunloye, for example, fails explicitly to recognize that varying the specific *weight* ratios of individual the inner or outer layers with respect to the core (claims 5 and 6), varying the core *weight* percentage of a disintegrating agent (claim 1, previously claim 8), varying the core *weight* percentage of the amino and organic acids (claims 9-11), or varying the core *diameter* and *thickness* (claim 14) could result in a preparation, which "in a disintegration test comprising vertical movement for 2 hours in a first solution of pH 1.2, subsequent vertical movement for 2 hours in a second solution of pH 7.4, and final vertical movement in a third solution of pH 6.4, the average disintegration initiation time and the average disintegration completion time each fall within a period from 35 min to 130 min after starting the vertical movement in the third solution."

Regarding claims 5 and 6, although Tanida teaches absolute material amounts of inner and outer layers depending on the *size* of the capsule, *see* col. 4, line 42 through col. 5, line 2, relative weight amounts between the layers and a core are not taught as important for disintegration time. In fact, Tanida, by expressing varying sized capsules tends to teach away from any linkage between core dimension or layer-to-core weight ratios and disintegration time, by emphasizing weight to size relationships without any regard to capsule weight. *See* Tanida col. 4 at lines 42-45 ("Said coating amount may vary depending upon the size of the capsule… Thus, the amount for inner layer… and that for outer layer… vary depending upon size of the capsule"); *see also*, Tanida col. 4 at lines 59-64 ("Since there are capsules of various sizes… in terms of the coating amount to the surface area of the capsule.")

Specifically regarding previous claim 8, none of the references teach 3-15 weight % of any of the disintegrating agents, which feature is now added to claim 1. *See* claim 1 ("crospovidone, pregelatinized starch, sodium carboxymethyl starch, carmellose, calcium, carmellose, sodium carmellose, powdered agar, sodium croscarmellose, low-substituted hydroxypropyl cellulose, starch, dextrin, hydroxyethylmethyl cellulose, carboxymethyl cellulose, hydroxypropyl starch, Macrogol,

and mannitol."); *compare* with Tanida's Eudragit E and Eudragit S, which are not in previous claim 8, at 7%; and crospovidone at 50% by weight.

Regarding claims 9-11, Adesunloye teaches acid amounts only to affect a reduction in cross-linking, but never to maximize disintegration time properties.

Applicants also therefore submit that the current claims are not obvious in view of Applicants' discovery that "merely specifying and optimizing the type and the thickness of the polymer covering the core is not sufficient; the disintegration properties of the final preparation are affected by the physicochemical properties of the tablet or capsule used as the core" and of "preparation disintegration test conditions for specifying a preparation that reliably guarantee the human colon disintegration performance and physical properties that the preparation should have under the test conditions." *See* paragraphs [0005] and [0011] of the published application, respectively. "[A] patentable invention may lie in the discovery of the source of a problem even though the remedy may be obvious once the source of the problem is identified. This is part of the 'subject matter as a whole' which should always be considered in determining the obviousness of an invention under 35 U.S.C. § 103." *In re Sponnoble*, 405 F.2d 578, 585, 160 USPQ 237, 243 (CCPA 1969)." MPEP § 2141.02 (III).

By way of a clear and persuasive assertion in the specification, Applicants show that the subject matter claimed is not obvious, in part, because it is in solution of a problem that they discovered. "[T]he formulation for a tablet or a capsule used as a core, in particular the type and amount of pharmacologically active material contained in the core, affects the disintegration properties." *See* paragraph [0005] of the published application; *see also,* paragraphs [0006]-[0011].

Thus, Applicants respectfully submit that the Examiner's statement that "the prior art appears to contain the exact same ingredients" improperly ignores the aforementioned limitations in the claims. Every limitation must be considered, moreover, without regard to its "gist" or "critical features". "Distilling an invention down to the "gist" or "thrust" of an invention disregards the

requirement of analyzing the subject matter "as a whole." *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984) (restricting consideration of the claims to a 10% per second rate of stretching of unsintered PTFE and disregarding other limitations resulted in treating claims as though they read differently than allowed)." MPEP § 2142.02(II); *In re Wilson*, 424 F.2d 1382, 1385 (CCPA 1970); *In re Royka*, 490 F.2d 981 (CCPA 1974); *Richardson v. Suzuki Motor Co.*, 868 F.2d 1226, 1236, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989) ("The identical invention must be shown in as complete detail as is contained in the... claim.").

In addition, "[i]n determining whether the invention as a whole would have been obvious under 35 U.S.C. 103, we must first delineate the invention as a whole. In delineating the invention as a whole, we look not only to the subject matter which is literally recited in the claim in question... but also to those properties of the subject matter which are inherent in the subject matter *and* are disclosed in the specification. Just as we look to a chemical and its properties when we examine the obviousness of a composition of matter claim, it is this invention *as a whole*, and not some part of it, which must be obvious under 35 U.S.C. 103." *In re Antonie*, 559 F.2d 618, 620, 195 USPQ 6,8 (CCPA 1977) (emphasis in original) (citations omitted) *See also In re Papesch*, 315 F.2d 381, 391, 137 USPQ 43, 51 (CCPA 1963) ("From the standpoint of patent law, a compound and all its properties are inseparable.").

Obviousness cannot be predicated on what is not known at the time an invention is made, even if the inherency of a certain feature is later established. *In re Rijckaert*, 9 F.2d 1531, 28 USPQ 1955 (Fed. Cir. 1993). MPEP § 2142.02 (V). Thus, even if the above-mentioned limitations are later held inherent, which they are not, the present claims would not be obvious over Tanida in view of Adesunloye because the presence of all of the claimed features could not have been known to one skilled in the art when Applicants invented the claimed invention.

As such, none of the experimental procedures and technical complexities by which the presently claimed invention was produced fall within the skill of one having skill in the art. Thus,

the combination of the cited references does not disclose or suggest a preparation characterized by any of claims 1-7 and 9-14.

For all of the foregoing reasons, Applicants respectfully submit that claims 1-7 and 9-14 are in condition for allowance, and accordingly, withdrawal of this rejection is respectfully requested.

CONCLUSION

A Notice of Allowance is respectfully requested. The Examiner is requested to call the undersigned at the telephone number listed below if this communication does not place the case in condition for allowance.

If this response is not considered timely filed and if a request for an extension of time is otherwise absent, Applicant hereby requests any necessary extension of time. If there is a fee occasioned by this response, including an extension fee, that is not covered by an enclosed check, please charge any deficiency to Deposit Account No. 23/2825.

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Respectfully submitted,

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